

**Table S4.** Results from Mann-Whitney U tests after Benjamini–Hochberg corrections for differences in relative abundance between *APOE 3* and *APOE 4* in young mice samples, old mice samples and both age groups.

| Taxa          |   | Young mice |                          |                          | Old mice |                          |                          | Young & Old mice |                          |                          |
|---------------|---|------------|--------------------------|--------------------------|----------|--------------------------|--------------------------|------------------|--------------------------|--------------------------|
|               |   | adj.p      | mean<br>( <i>APOE3</i> ) | mean<br>( <i>APOE4</i> ) | adj.p    | mean<br>( <i>APOE3</i> ) | mean<br>( <i>APOE4</i> ) | adj.p            | mean<br>( <i>APOE3</i> ) | mean<br>( <i>APOE4</i> ) |
| <i>Phylum</i> | Candidatus Saccharibacteria   | 0.002      | 0.48                     | 0.08                     | 0.372    | 0.33                     | 0.18                     | 0.000            | 0.43                     | 0.12                     |
|               | Deferribacteres   | 0.001      | 0.16                     | 0.61                     | 0.030    | 0.35                     | 1.57                     | 0.000            | 0.23                     | 0.97                     |
|               | Proteobacteria  | 0.000      | 1.71                     | 0.86                     | 0.396    | 4.27                     | 4.11                     | 0.594            | 2.67                     | 2.08                     |
| <i>Class</i>  | Deferribacteres.Deferribacteres   | 0.003      | 0.16                     | 0.61                     | 0.061    | 0.35                     | 1.57                     | 0.000            | 0.23                     | 0.97                     |
|               | Firmicutes.Erysipelotrichia   | 0.029      | 0.67                     | 0.04                     | 0.312    | 2.18                     | 5.28                     | 1.000            | 1.23                     | 2.01                     |
|               | Proteobacteria.Deltaproteobacteria  | 0.023      | 1.03                     | 0.45                     | 0.452    | 1.84                     | 3.34                     | 1.000            | 1.33                     | 1.53                     |
| <i>Order</i>  | Deferribacteres.Deferribacteres.Deferribacterales                                       | 0.003      | 0.16                     | 0.61                     | 0.065    | 0.35                     | 1.57                     | 0.000            | 0.23                     | 0.97                     |
|               | Firmicutes.Clostridia.Clostridiales   | 0.020      | 42.39                    | 56.34                    | 1.000    | 68.93                    | 67.65                    | 1.000            | 52.34                    | 60.58                    |
|               | Firmicutes.Erysipelotrichia.Erysipelotrichales  | 0.032      | 0.67                     | 0.04                     | 0.338    | 2.18                     | 5.28                     | 1.000            | 1.23                     | 2.01                     |
|               | Proteobacteria.Deltaproteobacteria.Desulfovibrionales                                   | 0.025      | 1.03                     | 0.45                     | 0.494    | 1.84                     | 3.34                     | 1.000            | 1.33                     | 1.53                     |
| <i>Family</i> | Bacteroidetes.Bacteroidia.Bacteroidales.Bacteroidaceae                                  | 0.001      | 0.89                     | 0.28                     | 0.058    | 8.96                     | 0.35                     | 0.000            | 3.92                     | 0.31                     |
|               | Bacteroidetes.Bacteroidia.Bacteroidales.Prevotellaceae                                  | 0.038      | 1.76                     | 0.79                     | 1.000    | 0.03                     | 0.00                     | 1.000            | 1.11                     | 0.49                     |
|               | Bacteroidetes.Bacteroidia.Bacteroidales.Rikenellaceae                                   | 0.015      | 3.98                     | 2.01                     | 1.000    | 3.10                     | 3.84                     | 0.319            | 3.65                     | 2.70                     |
|               | Deferribacteres.Deferribacteres.Deferribacterales.Deferribacteraceae                    | 0.005      | 0.16                     | 0.61                     | 0.108    | 0.35                     | 1.57                     | 0.000            | 0.23                     | 0.97                     |
|               | Firmicutes.Clostridia.Clostridiales.Clostridiales Incertae Sedis XIII                   | 0.048      | 0.00                     | 0.01                     | 1.000    | 0.01                     | 0.01                     | 0.909            | 0.00                     | 0.01                     |
|               | Firmicutes.Clostridia.Clostridiales.Lachnospiraceae                                     | 0.002      | 30.93                    | 47.83                    | 1.000    | 43.80                    | 43.34                    | 0.039            | 35.76                    | 46.15                    |
|               | Firmicutes.Erysipelotrichia.Erysipelotrichales.Erysipelotrichaceae                      | 0.048      | 0.67                     | 0.04                     | 0.545    | 2.18                     | 5.28                     | 1.000            | 1.23                     | 2.01                     |
|               | Proteobacteria.Deltaproteobacteria.Desulfovibrionales.Desulfovibrionaceae               | 0.000      | 0.00                     | 0.26                     | 1.000    | 1.80                     | 1.72                     | 1.000            | 0.68                     | 0.81                     |
| <i>Genus</i>  | Actinobacteria.Actinobacteria.Coriobacteriales.Coriobacteriaceae.Enterorhabdus          | 0.057      | 0.10                     | 0.40                     | 1.000    | 0.10                     | 0.13                     | 0.043            | 0.10                     | 0.30                     |
|               | Bacteroidetes.Bacteroidia.Bacteroidales.Bacteroidaceae.Bacteroides                      | 0.002      | 0.89                     | 0.28                     | 0.104    | 8.96                     | 0.35                     | 0.000            | 3.92                     | 0.31                     |
|               | Bacteroidetes.Bacteroidia.Bacteroidales.Porphyromonadaceae.Odoribacter                  | 0.720      | 0.42                     | 0.80                     | 0.104    | 0.18                     | 1.92                     | 0.001            | 0.33                     | 1.22                     |
|               | Bacteroidetes.Bacteroidia.Bacteroidales.Rikenellaceae.Alistipes                         | 0.028      | 3.98                     | 2.01                     | 1.000    | 3.10                     | 3.84                     | 0.577            | 3.65                     | 2.70                     |
|               | Deferribacteres.Deferribacteres.Deferribacterales.Deferribacteraceae.Mucispirillum      | 0.009      | 0.16                     | 0.61                     | 0.195    | 0.35                     | 1.57                     | 0.000            | 0.23                     | 0.97                     |
|               | Firmicutes.Clostridia.Clostridiales.Lachnospiraceae.Clostridium XIVa                    | 0.171      | 0.97                     | 1.94                     | 1.000    | 1.05                     | 2.33                     | 0.032            | 1.00                     | 2.09                     |
|               | Firmicutes.Clostridia.Clostridiales.Lachnospiraceae.Johnsonella                         | 0.011      | 0.02                     | 0.00                     | 1.000    | 0.04                     | 0.60                     | 1.000            | 0.03                     | 0.22                     |
|               | Firmicutes.Clostridia.Clostridiales.Ruminococcaceae.Butyricicoccus                      | 0.001      | 0.08                     | 0.32                     | 1.000    | 0.07                     | 0.19                     | 0.000            | 0.08                     | 0.27                     |
|               | Proteobacteria.Deltaproteobacteria.Desulfovibrionales.Desulfovibrionaceae.Desulfovibrio | 0.001      | 0.00                     | 0.26                     | 1.000    | 1.80                     | 1.72                     | 1.000            | 0.68                     | 0.81                     |